Amendments to the Specification:

Please replace the paragraph on page 12 beginning with line 1 with the following amended paragraph:

Figure ~~9 (top)~~ 9A shows domain analysis of the amino acid sequence of SUP protein. The protein sequence is broken down into the ubiquitin-associated domain, the ubiquitin protease domain, and the response regulatory domain. The catalytic cysteine active site with a conserved cysteine residue which is characteristic of ubiquitin specific protease domains is indicated. The PKC site is indicated. The tyrosine phosphorylation site is indicated. The active site conserved histidines characteristic of ubiquitin specific protease domains are indicated.

Please replace the paragraph on page 12 beginning with line 8 with the following amended paragraph:

Figure ~~9 (bottom)~~ 9B shows Northern blot of USP-25 mRNA expression in human tissue samples and human cancer cell lines.

Please replace the paragraph on page 12 beginning with line 11 with the following amended paragraph:

~~Figure 10 (top) shows~~ Figures 10A and 10B show catalytically inactive USP-25 C to S mutant blocks TCR-induced expression of luciferase reporter gene fused to NFAT gene promoter in transfected cells. Cells transfected with USP-25 C to S catalytic mutant "SUP(C>S)", USP-25 wildtype "SUPwt", or empty vector pEFnig. USP-25 C to S catalytic mutant also referred to herein as dominant negative USP-25 protein variant or grammatical equivalents. Luciferase activity is shown in Figure 10A and is determined in cells exposed to different concentrations of C305 (0, 100, 300, 1000ng/mL0 which activates TCR. Western blots "wb" showing protein expression in cells are also provided in Figure 10B.

Please replace the paragraph on page 12 beginning with line 19 with the following amended paragraph:

Figure ~~10 (bottom)~~ 10C shows USP-25 C to S catalytic mutant inhibits NFAT promoter activity by acting downstream of calcium signaling. Cells in the presence or absence of phorbol ester and calcium ionophore (PMA+iono, + or -) and transfected with expression vectors encoding

USP-25 C to S catalytic mutant "SUPmt" or USP-25 wildtype "SUPwt" or empty vector. NFAT promoter fused to luciferase reporter gene and luciferase activity determined.

Please replace the paragraph on page 12 beginning with line 25 with the following amended paragraph:

~~Figure 11 (top) shows~~ Figure 11A and 11B show USP-25 C to S catalytic mutant does not affect AP-1 activation by TCR activation or phorbol ester and calcium ionophore. AP-1 responsive elements fused to luciferase reporter gene in cells transfected with empty vector "PCDEF-nig", wildtype USP-25 "SUPwt-nig", USP-25 C to S catalytic mutant "SUP(C>M)-nig", or PAK2L "PAK2L-nig". In the presence or absence of phorbol ester and ionomycin (PMA/iono + or -), luciferase activity determined, as shown in Figure 11B. Cells exposed to different concentration of C305 (0ng/mL, 100ng/mL, 300ng/mL) which activates TCR, and luciferase activity determined, as shown in Figure 11A.

Please replace the paragraph on page 12 beginning with line 33 with the following amended paragraph:

~~Figure 11 (bottom) shows~~ Figure 11C-11N show catalytically inactive USP-25 does not affect TCR-induced calcium flux. FACS analysis of cells transfected with empty vector "PCDEF nig vector" Figures 11C-11E, or expression vector encoding wildtype USP-25 "PCDEF SUP wt" Figures 11F-11H, or USP-25 C to S catalytic mutant "PCDEF SUP mutant" Figures 11I-11K, or TRAC "PCDEF TRAC" Figures 11L-11N.

Please replace the paragraph on page 12 beginning with line 38 with the following amended paragraph:

~~Figure 12 (top) shows~~ Figures 12A-12L show USP-25 C to S catalytic mutant does not affect CD69 expression. FACS analysis of cells transfected with empty vector "pEFnig", or expression vector encoding wildtype USP-25 protein "SUP-wt", USP-25 C to S catalytic mutant "SUP(C>S)" or PAK2L "PAK2L", and exposed to different concentrations of C305 (0, Figures 12A-12D; 100 ng/mL, Figures 12E-12H; and 300 ng/mL, Figures 12I-12L;) which activates TCR.

Please replace the paragraph on page 13 beginning with line 4 with the following amended paragraph:

~~Figure 12 (bottom) shows~~ Figures 12M and 12N show N-terminal USP-25 truncation mutants inhibit NFAT promoter activity. ~~The figure~~ Figure 12M shows the structure of wildtype USP-25 and three N-terminal truncation mutants thereof (58-1060, 659-1060, and 861-1060). NFAT promoter is linked to luciferase reporter gene and luciferase activity is determined in cells transfected with empty vector "pEFnig" or expression vectors encoding wildtype USP-25 "SUP-wt", or one of the three indicated N-terminal truncations mutants thereof, or SLIM "SLIM nig", and exposed to different concentrations of C305 (0, 100ng/mL, 300ng/mL, 1000ng/mL) which activates TCR. Figure 12N shows the results of the lucifierase assay.

Please replace the paragraph on page 13 beginning with line 12 with the following amended paragraph:

Figure ~~13 (top)~~ 13A shows USP-25 C to S catalytic mutant inhibits NFAT activity in BJAB cells. NFAT promoter is fused to luciferase reporter gene and luciferase activity is determined in cells transfected with empty vector "pEFnig", or expression vector encoding wildtype USP-25 "SUP-wt", or one of three N-terminal truncation mutants thereof and described in Figure 12 (bottom), or USP-25 C to S catalytic mutant "SUP(C>S)", or SLIM "SLIMnig", and exposed to varied concentrations of anti-IgM antibody (0, 100 ng/mL, 300 ng/mL).

Please replace the paragraph on page 13 beginning with line 12 with the following amended paragraph:

Figure ~~13 (bottom)~~ 13B is a schematic depiction of the possible regulatory role of USP-25 on the NFAT promoter.